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(56) Documents Cited

US 4099923 A
WPI Acc. No. 86-212588/198633 & DD 0234942 A
Angewandte Chem. Int. Edition Eng. 1996, 35, No.2,
pages 220 to 222

(58) Field of Search

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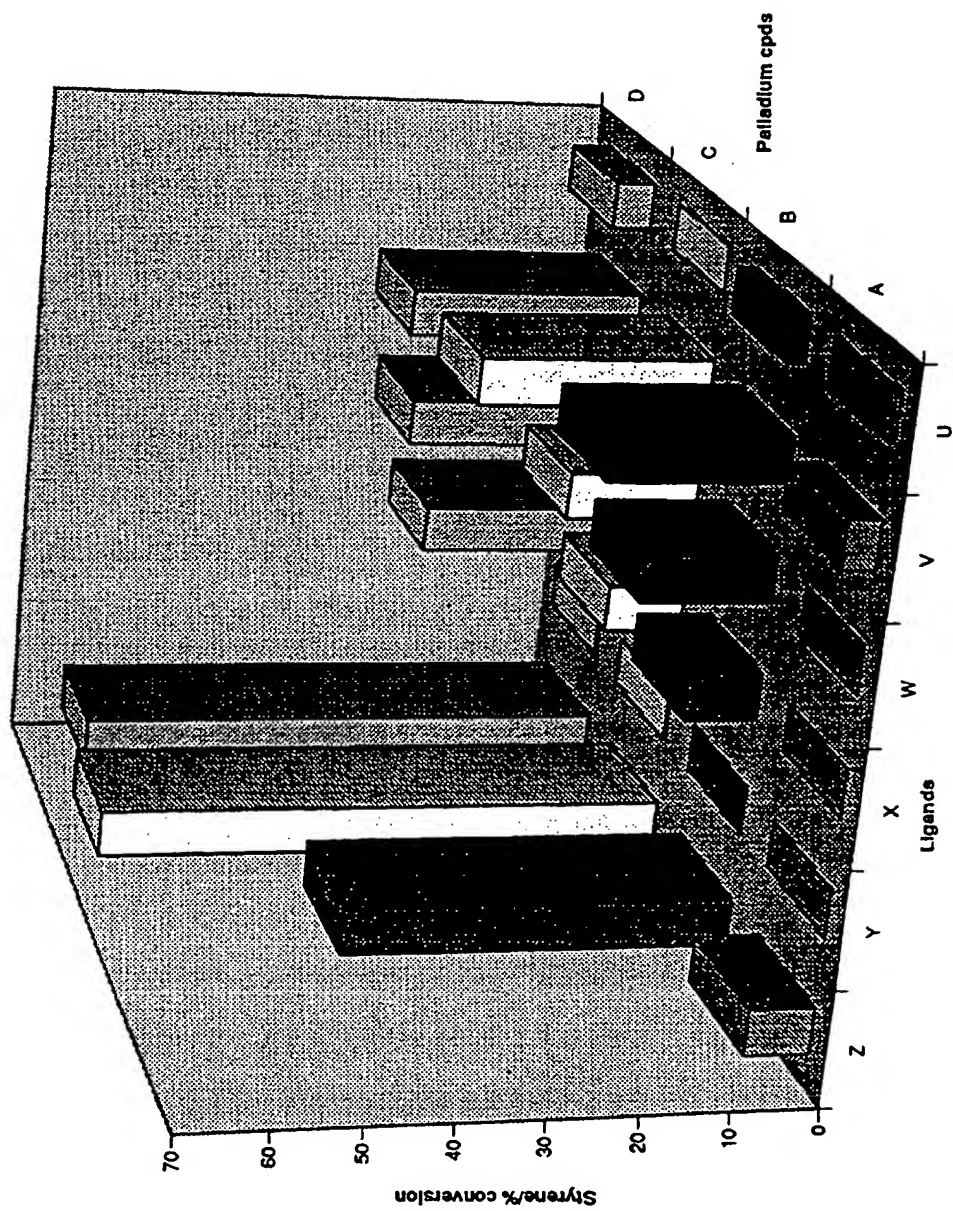
(54) Abstract Title

Catalyst screening system

(57) A catalyst testing device incorporates an array of identical reaction cells for batches of liquid phase reactants, combined with a sensor means capable of monitoring at least one characteristic of the progress of a selected catalyst reaction. Catalysts are tested for a particular reaction by dosing samples of liquid phase reactants into a plurality of reaction cells, dosing different test catalysts into each cell and determining the progress of each catalytic reaction in each cell using the same measurand.

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A comparison of catalysts in the production of styrene



IMPROVEMENTS IN CATALYST TESTING

This invention concerns improvements in catalyst testing, and more especially concerns a homogeneous catalyst testing kit and method.

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The development of catalysts is generally a painstaking sequential exercise. Recently, a combinational method has been disclosed in Angew. Chem. Int. Ed. Engl. 1996, 35 No 2 pp220-222, in which 96-section systems were examined simultaneously by utilising a microtitre plate format. After a reaction period, the reactant/product compositions were analysed using an HPLC equipped with an autosampler. It was stated that preliminary results could be obtained in less than a week. For industrial development, however, it is desirable to reduce the time to much less than a week. Preliminary studies leading to the present invention show a complete assessment of a 24-cell study in less than a day, and it is estimated that an optimised apparatus is capable of completing an assessment in a few hours.

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There are many chemical reactions of industrial importance which require a homogeneous catalyst, for example Pd-mediated coupling reactions, hydrogenation, hydroformylation, isomerisation and many chiral catalysed reactions.

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To a great extent, such reactions utilise the first catalyst tested and published. It is frequently impossible to predict, however, the effectiveness of new homogeneous catalysts for any particular reaction or reaction system. In light of the economic importance of catalytic reactions, there remains a great need for new catalysts or new applications for known homogeneous catalysts.

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The present invention provides catalyst testing apparatus consisting essentially of a multiplicity of identical reaction cells for batches of liquid phase reactants in combination with sensor means capable of monitoring at least one measurand which is characteristic of either one or more catalytic reactions or the kinetics thereof.

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The invention also provides a method of testing homogeneous catalysts for a catalytic reaction, comprising forming a volume of liquid phase reactants, dosing said volume into a multiplicity of identical reaction cells, dosing a different homogeneous catalyst or precursor into each cell and admixing it with the reactants and monitoring each cell using the same measurand to determine the progress of the catalytic reaction in each cell.

In its most basic form, the sensor means may be a single sensor or analytical equipment with the provision to sense the measurand applicable to each batch of reactant, sequentially. The sensor or equipment may be moved from cell to cell or the cells, or samples from the cells, may be fed in sequence to the sensor or equipment. The apparatus preferably incorporates automatic feeding equipment and computer-control effective either to sample each cell at the same time or to freeze the catalytic reaction at the same point for subsequent sensing or analysis.

The sensor or analytical equipment may be one or more of a gas chromatograph, high performance liquid chromatograph, NMR spectrometer, absorption spectrometer or colorimetric analyser optionally using an indicator capable of detecting quantities of a desired reaction product or the consumption of a reactant. Microcalorimetry may also be used to measure the kinetics of the reaction. In such a way, a clear assessment may be made of the progress of each catalytic reaction in each cell, and hence, which catalytic system is most effective under the reaction conditions.

Preferably, the apparatus comprises temperature control means, for example incorporating a temperature controlled liquid bath isolated from the sample cells, and also comprises agitation means to permit simultaneous mixing of catalyst samples with the reactants. More preferably, the apparatus also comprises thermal insulation sufficient to permit microcalorimetric measurement. Ideally, therefore, the apparatus permits two or more assessment methods to be chosen according to the reaction being studied.

The apparatus may comprise an array of 24, 96 *etc* identical reaction cells, the volume of which may be from 0.05 to 5ml. A preferred apparatus includes simultaneous dosing

means to place identical quantities of the reactants in each cell, and the same or different dosing means may be used to dose identical quantities (identical volumes of identical concentration catalyst solutions or precursors thereof, or of different concentrations, as required) of the different catalysts into each cell. The apparatus may also comprise means
5 for dosing a substance at the end of a selected reaction period, for example to quench the reaction or to absorb a reactant or product, depending upon reaction rate considerations.

In certain embodiments, there may be gas supply means capable of supplying gaseous reactants *etc* to the reaction cells as a whole or individually.

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A preferred embodiment of the present invention incorporates one or more sensor elements in each of the cells. A particularly preferred sensor is a temperature sensor, which may be a thermocouple, a thermistor such as a platinum resistance thermometer, or some other temperature sensor capable of monitoring the progress of a catalytic reaction.
15 Although temperature sensors are preferred, other sensors such as pH sensors, conductivity sensors, ion selective electrodes may be used in addition or as substitutes for temperature sensing. Each cell may incorporate, in a further embodiment, one or more optical fibre leads which are capable itself as acting as a sensor or as an activator, light source *etc* for the sensor.

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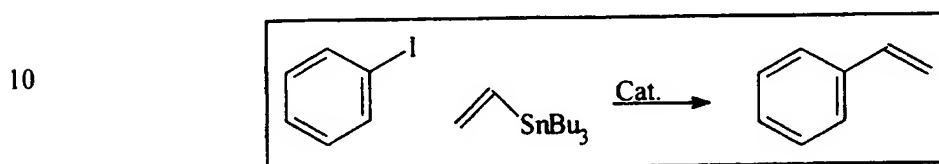
The apparatus preferably includes timing means, which may conveniently be a feature of a microprocessor controller, to activate or to read the sensor means. Reading the sensor means may be carried out at a fixed time point, at a number of fixed time points, or continuously. Recording means and display means are desirably included, which may be in
25 the form of computer memory together with a visual display, or a hard copy output *eg* a paper trace.

It can readily be seen that the invention provides an extremely economic and rapid assessment of a large number of homogeneous catalysts in a way that has not previously
30 been attempted. The skilled synthetic chemist is able to make small quantities, often just μg

quantities, of prospective homogeneous catalysts in a systematic way and these may be screened using the method and apparatus of the invention.

The invention is described further in the following Example which is by way of illustration only and is not intended to be limiting.

EXAMPLE



The Stille coupling of iodobenzene with vinyltributyltin was chosen as a model reaction for this approach of selecting the optimum catalyst for a given reaction. This reaction has been used to ascertain the mechanism of the coupling and a comprehensive study of the effect of ligand has been published (V Farina and B Krishnan, *Journal of the American Chemical Society*, 1991, 113, 9585-9595). In this paper palladium/ligand combinations were studied sequentially. The reaction was carried out at 50°C and the catalyst generated in situ from Pd₂dba₃ and four equivalents/Pd of triphenylarsine gave the fastest rate under the conditions selected. As a test of our technique we sought to optimise catalysts further by identifying a Pd precursor/ligand combination which would give acceptable conversion at room temperature.

25 Stock solutions of reactants and catalysts were made up under argon in thf so that in 1ml of solution, the required amount of reactant/catalyst (Pd precursor 0.009mmol, ligand 0.036mmol, iodobenzene 0.892mmol) could be added to each vial. Also a stock solution of thiourea in water was made to quench the reaction so that 10μl contained 0.09mmol. Palladium precursors used were A Pd₂dba₃ (dba = dibenzylideneacetone, *trans,trans*-1,5-diphenyl-1,4-pentadien-3-one), B *trans*-bis(benzonitrile)dichloropalladium(II), C Pd(acac)₂ (acac = acetylacetonate) and D palladium acetate trimer. Ligands used were U tris(2,4,6-

trimethylphenyl)phosphine, **V** tris(morpholino)phosphine, **W** tris(2-furyl)phosphine, **X** triphenylphosphite, **Y** tris(2,6- dimethoxyphenyl)phosphine and **Z** triphenylarsine

5 Twenty-four vials were set up in an argon glove-box (four different palladium compounds with six different ligands) and in each vial 1ml of iodobenzene solution was added. Then 1ml of the appropriate ligand solution was added followed by 1ml of palladium precursor solution to each vial to give twenty-four vials, each containing a different catalyst solution. Vinyltributyltin (0.3ml, 1.026mmol) was then added to each vial, the vials were sealed, left for 17 hours then quenched with thiourea solution (10 μ l).

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The conversion to styrene was measured by gas chromatograph and results are shown graphically in Figure 1. Under the conditions of this experiment it is clear that the best catalysts are those based on Pd (II) precursors, rather than the Pd (0) precursor suggested in the literature, although triphenylarsine is again the ligand which gives rise to the most active
15 catalysts.

CLAIMS

1. A catalyst testing apparatus consisting essentially of a multiplicity of identical reaction cells for batches of liquid phase reactants in combination with sensor means capable
5 of monitoring at least one measurand which is characteristic of either one or more catalytic reactions or the kinetics thereof.
2. Apparatus according to claim 1, wherein the measurand is characteristic of the quantity of a reaction product produced or the quantity of a reactant consumed.
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3. Apparatus according to claim 1 or 2, wherein temperature sensing is provided to measure the temperature of the reactants.
4. Apparatus according to claim 3, wherein each reaction cell is provided with a
15 temperature sensor.
5. Apparatus according to any one of the preceding claims, comprising also temperature control means and/or agitation means.
- 20 6. Apparatus according to any one of the preceding claims, comprising also means to insulate each reaction cell and means to carry out microcalorimetric measurement.
7. Apparatus according to any one of the preceding claims, comprising also dosing means to charge each cell with identical quantities of liquid phase reactants.
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8. Apparatus according to claim 7, comprising also dosing means to charge different catalysts or catalyst precursors into each cell.
9. A method of testing homogeneous catalysts for a catalytic reaction, comprising
30 forming a volume of liquid phase reactants, dosing said volume into a multiplicity of identical reaction cells, dosing a different homogeneous catalyst or precursor therefor into

each cell and admixing it with the reactants, and monitoring each cell using the same measurand to determine the progress of the catalytic reaction in each cell.

10. A method according to claim 9, wherein the measurand is temperature.
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11. A homogeneous catalyst developed by the testing method of claim 9 or 10.
12. A homogeneous platinum group metal catalyst developed by the testing method of claim 9 or 10.



Application No: GB 9715731.7
Claims searched: 1 - 12

Examiner: Michael R. Wendt
Date of search: 29 September 1997

Patents Act 1977
Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK CI (Ed.O): G1B (BAA, BBC, BCX)

Int CI (Ed.6): G01N 31/10

Other: Online: WPI, Claims, Japio

Documents considered to be relevant:

Category	Identity of document and relevant passage	Relevant to claims
X	US 4099923 (STANDARD OIL) e.g. see Claim 1 & Figure 1.	1 & 9
X	WPI Accession No. 86-212588/198633 & DD 0234942 A (VL-W ULBRICHT) see Abstract.	1 & 9
X	Angewandte Chem. Int. Edition Eng. 1996, 35, No. 2, pages 220 - 222. (Burgess et al) - referred to in application.	1 & 9

X Document indicating lack of novelty or inventive step
Y Document indicating lack of inventive step if combined with one or more other documents of same category.
& Member of the same patent family

A Document indicating technological background and/or state of the art.
P Document published on or after the declared priority date but before the filing date of this invention.
E Patent document published on or after, but with priority date earlier than, the filing date of this application.